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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
SULLIVAN, DANIEL M

ART UNIT	PAPER NUMBER
1636	

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13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/831,907	BEAUVILLAIN ET AL.	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *3-8 and 11-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,9,10,14 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 September 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This is the First Office Action on the Merits of this U.S. National stage filing of international application PCT/FR99/02941 filed 26 November 1999, which claims priority to French Patent Application 9814914 filed 26 November 1998. Claims 1-15 are pending in the application.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1, 2, 9, 10, 14 and 15 in Paper No. 12, filed 16 January 2003, is acknowledged. The traversal is on three grounds. First, Applicant argues the claims of Groups I-IV and VIII-X depend directly from the claims of Group I, and as such clearly share a common special technical feature. This argument is not persuasive because the claims of Groups II-IV and VIII-X depend from the claims of Group I only in that the nucleic acids are limited to being derived from a nucleic acid encoding the polypeptides of Group I. The claims are clearly directed to different molecules because the claims of Group I are directed to polypeptides while the claims of Group II are directed to nucleic acids or a method of using a nucleic acid, structurally and functionally distinct molecules.

Next, Applicant argues that the International Preliminary Examination Authority did not find lack of unity. However, 37 CFR § 1.499 states, "[i]f the examiner finds that a national stage application lacks unity of invention under § 1.475, the examiner may in an Office action require the applicant in the response to that action to elect the invention to which the claims shall be restricted. Such requirement may be made before any action on the merits but may be made at any time before the final action at the discretion of the examiner. Review of any such

requirement is provided under § § 1.143 and 1.144." The rules clearly indicate that restriction if proper at any time in prosecution at the examiners discretion and do not in any way indicate that the Examiner in the national stage is bound by any findings by the International Examination Authority.

Finally, Applicant cites MPEP 803, which states that if a search of an entire application can be made without a serious burden the examiner must examine it on the merits, and submits that the finding of lack of unity is improper because a search of the claims would not impose a serious burden on the Office. This argument is not persuasive because it confuses the requirements of U.S. restriction practice, set forth in MPEP 803, with the requirements for lack of unit, which are found in MPEP 1800, and do not set forth burden of search as a factor in a finding of lack of unity. Furthermore, the rejoinder of the groups would clearly impose an additional search burden on the Office because the proteins of Group I would not be found in the same database as the Nucleic acids of Group II. Therefore the claims would have to be searched separately.

The requirement is still deemed proper and is therefore made FINAL.

Claims 3-8 and 11-13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. Applicant timely traversed the restriction requirement in Paper No. 12.

Drawings

The drawings are objected to because the word "human" is misspelled in Figure 1. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Specification

The disclosure is objected to because of the following informalities: Figures 1-4 contain sequence disclosures without accompanying sequence identifier numbers (SEQ ID NO). The brief description of the drawings should be amended to include SEQ ID NO's that indicate which of the sequences in the Sequence Listing correspond to the sequences set forth in the figures.

Appropriate correction is required.

Claim Objections

Claims 9 and 10 are objected to because of the following informalities: The claims, as they are directed to compositions comprising and methods of using nucleic acids, encompass non-elected subject matter, which should be deleted from the claims. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 10 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

Claims 1, 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide comprising the sequences set forth as SEQ ID NO:1-3, 30-32 and 33-35 and a method of using said polypeptides for identifying anti-hypertensive agents, does not reasonably provide enablement for any and all polypeptides comprising at the C-terminal end the sequence Cys-Phe-Trp-Lys-Tyr-Cys-Xaa, wherein Xaa represents Val or Ile, and having 45% or 70% similarity with the polypeptide of SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to

make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the invention: The claims of the instant invention are directed to polypeptides that are structurally related to mammalian urotensin II polypeptides, and methods of using said polypeptides.

Breadth of the claims: The polypeptides of the claims encompass a large genus of structurally divergent polypeptides wherein any given amino acid can be substituted with at least any of the 25 other naturally occurring amino acids in any combination, so long as the polypeptide comprises the sequence Cys-Phe-Trp-Lys-Tyr-Cys-Xaa at it's C-terminus and meets the limitation of 45% or 70% similarity to SEQ ID NO:1. Because the polypeptide is not limited to a polypeptide having any disclosed function, the claims encompass many polypeptides of unknown function.

State of the prior art and level of predictability in the art: The relevant art (e.g., Coulouarn *et al.* (1998) *Proc. Natl. Acad. Sci. USA* 95:15803-15808; made of record in the IDS filed 9 October 2001) teaches that the cyclic heptapeptide Cys-Phe-Trp-Lys-Tyr-Cys-Val is highly conserved in proteins having the function of a urotensin II, and that urotensin II molecules from various species are divergent in their N-terminal portion. The art further teaches that the active urotensin II polypeptide is produced by cleavage from the precursor polypetide. The teachings from the art do not, however, indicate that all polypeptides, or even a fraction of polypeptides comprising the sequence Cys-Phe-Trp-Lys-Tyr-Cys-Xaa at their C-terminus would have the functional characteristics set forth for urotensin II. In fact, given that urotensin II must

be processed to its active form, it is unlikely that molecules that lack appropriate processing signals would produce active peptides.

Amount of direction provided by the inventor and existence of working examples: With regard to how to use the full genus of claimed polypeptides, the instant disclosure does not teach how to use a polypeptide that does not have urotensin II function or how the skilled artisan might identify molecules having urotensin II function without trial and error experimentation to test each and every molecule encompassed by the claims.

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Although the level of skill in the art is high, the instant disclosure and prior art would not enable the skilled artisan to identify useful polypeptides within the claimed genus without testing each and every polypeptide for urotensin II activity or devising a use for each of the polypeptides not having the activity of urotensin II. As the genus encompasses many thousands of polypeptides and only a small fraction of these might be expected to have a useful function, the amount of experimentation required to use the full scope of the claimed invention would clearly be undue. Therefore, only the polypeptides set forth as SEQ ID NO: 1-3, 30-32 and 33-35 are adequately enabled by the disclosure.

Claims 9 and 10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to pharmaceutical compositions comprising urotensin II polypeptides and a method of treating neuordegenerative disease using urotensin II polypeptides. The disclosure (e.g., page 9, paragraph 5) provides that the instant polypeptides can be used to prepare a medicinal product intended to treat neurodegenerative diseases or traumas to the spinal chord. The claims thus encompass a pharmaceutical composition to be used for the purpose of treating neurodegenerative diseases or traumas to the spinal chord. The enabling disclosure must therefore teach the skilled artisan how to use the claimed pharmaceutical composition and practice the claimed method for the purpose of treating spinal chord neurodegeneration or trauma.

To the extent that the claims are directed to pharmaceutical compositions or methods of treatment comprising polypeptides other than those set forth as SEQ ID NO:1-3, 30-32 and 33-35, the claims are not enabled for the reasons set forth herein above.

With regard to treatment of neurodegenerative diseases or traumas to the spinal chord, the art provides no guidance. The relevant art merely teaches, "the functional significance of UII in motoneurons, especially in the human spinal chord, is currently a matter of speculation" (Coulouarn *et al.* page 15808, first full paragraph). Thus, the art teaches that, at the time of filing, there was no evidence that urotensin II could be used to treat neurodegenerative diseases or traumas to the spinal chord, and success in treating these conditions could not be predicted based on what was known at the time of filing. Therefore, the skilled artisan must rely solely on the teachings of the instant specification to enable treatment of neurodegenerative diseases or traumas to the spinal chord without undue experimentation. However, the specification provides no more guidance than the prior art. The disclosure points to the presence of urotensin II in the

spinal chord, among other tissues, and speculates that urotensin II might be used to treat neurodegenerative diseases or traumas to the spinal chord. The specification does not set forth a single process step involved in the method of treating neurodegenerative diseases or traumas to the spinal chord, provides no guidance with respect to effective dosage or routes of administration, and does not identify a single specific condition that would likely respond to treatment. Given that the art and specification fail to provided any evidence that urotensin II would have therapeutic efficacy in the treatment of neurodegenerative diseases or traumas to the spinal chord and provide no practical guidance as to how urotensin II polypeptides could be used in the treatment of neurodegenerative diseases or traumas to the spinal chord, the skilled artisan would have to engage in undue trial and error experimentation to develop the claimed composition and method to the point that it has practical utility. Thus using the claimed invention according to the teachings of the specification would clearly require the skilled artisan to engage in undue experimentation. Therefore, claims 9 and 10 are not enabled over any scope.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 9, 10 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2 and 9 are indefinite in their recitation of the sequence "Cys-Phe,Trp-..." It is not clear whether the use of a comma instead of a hyphen between Phe and Trp is intended to indicate other than a contiguous polypeptide sequence. Based on the disclosure, it would appear

that the comma is a typographical error and the claims have been examined on the merits with the assumption that the sequence should read "Cys-Phe-Trp-..."

Claim 10 is indefinite in being directed to a polypeptide that exhibits at least 45% and preferably at least 70% similarity with a polypeptide sequence of SEQ ID NO:1. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

In addition, claim 10 provides for the use of polypeptides belonging to the urotensin II family, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 14 is indefinite in being directed to a method of selecting anti-hypertensives wherein it appears that the compounds screened are limited to known anti-hypertensives (i.e., "determining the activity of an anti-hypertensive"). It is not clear whether the method is directed

to selecting known anti-hypertensives having urotensin II antagonist activity or directed to identifying new candidate anti-hypertensives based on antagonism of urotensin II.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 9, 14 and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Culp *et al.* U.S. Patent No. 6,075,137.

Culp *et al.* teaches a polypeptide comprising a the C-terminal end, a heptapeptide having the sequence Cys-Phe-Trp-Lys-tyr-Cys-Val and exhibiting at least 70% similarity to the polypeptide set forth as SEQ ID NO:1 according to the limitations of claims 1, 2 and 15 (see especially SEQ ID NO:2 and 4 and the attached sequence alignments).

Culp *et al.* further teaches a pharmaceutical composition comprising the disclosed polypeptide according to the limitations of claim 9 (see especially column 13, paragraph 1) and a method for screening for antagonists of urotensin II according to the method of claim 14 (see especially column 11-12). The polypeptide, composition and method taught by Culp *et al.* are the same as those taught in the instant application, therefore the limitations of the claims are met by Culp *et al.*

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-9105 for regular communications and 703-746-9105 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

dms
March 20, 2003

Anne-Marie Falke
ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER